

Applicant : Louis Casteilla
Luc Penicaud
Catherine Dacquet
Pierre Renard
Serial N°: US Serial No. 10/530,771
Filed : April 7, 2005
Title : Association between a ligand of peroxisome proliferators activated receptors and an antioxidant agent and pharmaceutical compositions containing them
Art Unit : 1614
Examiner : Savitha Rao

Honorable Commissioner of Patents
PO Box 1450
Alexandria VA 22313

DECLARATION Under 37 CFR 1.132

I, Catherine DACQUET, a citizen of France, of 116, rue Charles Le Bon, 59650 Villeneuve d'Ascq, France, declare and say that :

I am research project leader at the Les Laboratoires Servier, Paris. My interest of investigation consists of drug discovery research. I refer to my CV for an extensive overview of my backgrounds and qualifications, of which a copy is attached as Annex I.

I am the co-inventor of US Patent Application Serial n° 10/530,771 filed April 7, 2005 concerning "Association between a ligand of peroxisome proliferators activated receptors and an antioxidant agent and pharmaceutical compositions containing them".

I am thoroughly familiar with the above-mentioned patent application and fully support the pharmacological and chemical data contained therein which were performed either by me or under my supervision. I also fully support the conclusions derived and the arguments presented as concerns the therapeutic interest and utility of the associations described.

Two additional examples with regard to US Patent application n° 10/530,771 of association of 1) a mixed PPAR α /y ligand or a PPAR α and a PPARy ligand with 2) an antioxidant agent demonstrate the surprising effect of the associations according to the invention :

Common protocol to the two flowing examples :

Male C57 Black 6 ob/ob mice from 8 to 12 weeks old were used. After being placed in quarantine for one week, they were weighed and then randomised as a function of their weight and 6 homogeneous groups (starting weights not significantly different) were formed. After being weighed, the various compounds under test were injected by the intraperitoneal route once a day for 7 days. The compounds were injected in a solution of DMSO 5 % / Solutol 15 % / qsp H₂O heated at 65°C to ensure good dissolution. In

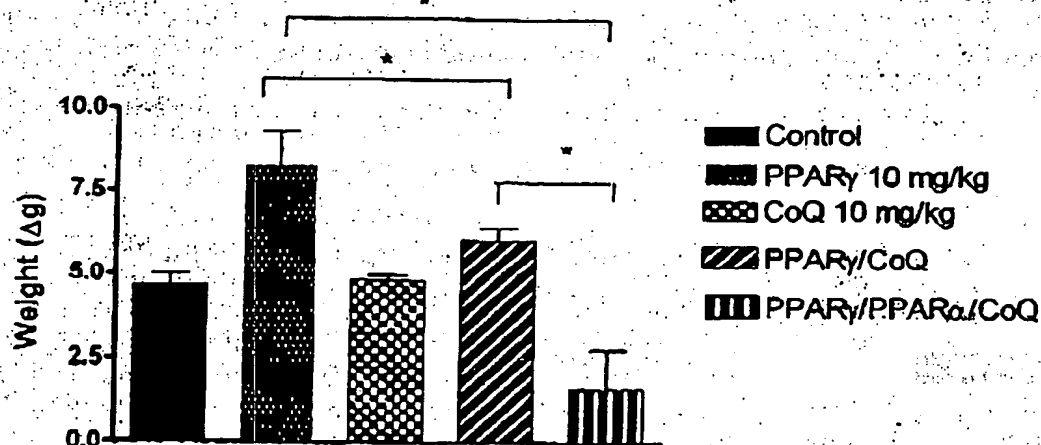
addition, the solution was pre-heated before injection. The mice were weighed every day and the weight obtained after 7 days of treatment was recorded.

Example 1 :

A reduction of 30 % is observed in the weight gain of mice treated with the association comprising 2-ethoxy-3-{4-[2-(6-[(hydroxyimino)(phenyl)methyl]-2-oxo-1,3-benzothiazol-3(2H)-yl)ethoxy]phenyl}propanoic acid which is a PPAR α / γ ligand and coenzyme Q₁₀, whereas coenzyme Q₁₀ administered on its own does not reduce the weight gain and 2-ethoxy-3-{4-[2-(6-[(hydroxyimino)(phenyl)methyl]-2-oxo-1,3-benzothiazol-3(2H)-yl)ethoxy]phenyl}propanoic acid administered on its own reduces the weight gain by only 10 %.

Example 2 :

The results obtained with the association of fenofibrate which is a PPAR α ligand + rosiglitazone which is a PPAR γ ligand + coenzyme Q₁₀ are indicated below and are expressed as the percentage weight change with respect to the control (corresponding to mice treated with the injection solvent for 7 days) :



Therefore, the results obtained from examples 1 and 2 clearly show :

- that the association enables the weight of obese mice to be reduced significantly,
- that there exists a synergy between the 2 or 3 components of the association, the weight loss found being much greater in the case of the association than in the case of each component administered on its own.

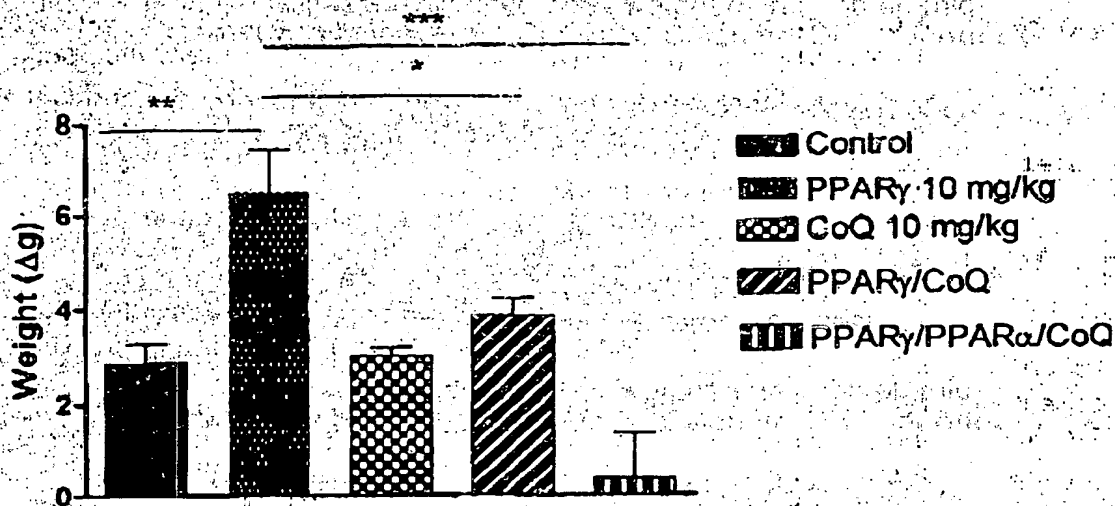
The following data correspond to quantitative data of example A in the description of the US patent n° 10/530,771. We observe that the weight of obese mice is reduced of 2.66g between mice treated with PPAR γ (6.52g \pm 0.91) and mice treated with PPAR γ + coenzyme Q₁₀ (3.86g \pm 0.36). Thus in view of these quantitative data, the weight loss is less or equal to 2.5 grams in accordance with the previous argument.

Control : 2.86 \pm 0.38 (n=8)

PPAR γ (Rosiglitazone) 10 mg/kg 6.52 \pm 0.91 (n= 7)

CoQ₁₀ mg/kg 2.98 \pm 0.18 (n=8)

PPAR γ (Rosiglitazone)/CoQ $_{10}$: 3.86 \pm 0.36 (n=6)
 PPAR γ (Rosiglitazone)/PPAR α /CoQ : 0.36 \pm 0.97 (n=6)



The associations of a mixed PPAR α/γ ligand or a PPAR α ligand and a PPAR γ ligand combined with an antioxydant disclosed in the invention have surprising properties in the treatment or prevention of obesity. Indeed, the associations enable the weight to be reduced significantly and allow a synergy between the 2 or 3 components of the association since the weight loss found being much greater in the case of the association than in the case of each component administered on its own. These surprising properties of these associations are confirmed and supported by the above comparative trials.

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that wilful false statements and the like so made are punishable by fine or imprisonment or both, under section 1001 of the title 18 of the United States Code and that such wilful false statements may jeopardize the validity of the application or any patent issued thereon.

Further declarant sayeth not

Catherine DACQUET

[Handwritten signature]

Executed at : Suresnes
 Date : January 8, 2009

Postal address
 LES LABORATOIRES SERVIER
 12, Place de La Défense
 92415 COURBEVOIE CEDEX
 FRANCE

ANNEX 1

CURRICULUM VITAE

Catherine Dacquet joined the Institut de Recherches Servier, Division of Molecular and Cellular Pharmacology in 1993 as a team leader where she was in charge of the screening of new compounds. She carried out assays development, test standardization using binding technology and several cellular systems. She then moved to the External Therapeutic Division in 1999 as a research project leader where she was in charge of the coordination of PPAR Research Project mainly focused to built a scientific network in partnerships with internal and external collaborations. She continue this project on the Division of Metabolic Disease since 2004 managing the in vitro and in vivo pharmacology. Prior to joining Servier, Catherine Dacquet was head of the laboratory of Pharmacology in Innothera, pharmaceutical industry specialized in the research of new molecules in the field of phlebologia. She had the responsibility of managing the drug discovery and the advanced projects to identify drugs for the treatment venous insufficiency. She obtained her Pharm D from the University of Bordeaux in 1984 and her PhD in 1988 with a thesis on the mechanism of the calcium antagonists on vascular voltage-dependent calcium channels.

1 Spedding M, Ouvre C, Millan M, Wurtman R, Duhault J & Dacquet C.
Neural control of dieting.
Nature, (1996),380, 488-489.

2 Milligan G, Kellett E, Dacquet C, Dubreuil V, Jacoby E, Millan MJ, Lavielle G, Spedding M.
S 14506: novel receptor coupling at 5-HT(1A) receptors.
Neuropharmacology. 2001 Mar;40(3):334-44.

3 Carmona MC, Louche K, Nibbelink M, Prunet B, Bross A, Desbazeille M, Dacquet C, Renard P, Castella L, Penicaud L.
Fenofibrate prevents Rosiglitazone-induced body weight gain in ob/ob mice.
Int J Obes (Lond). 2005 Jul;29(7):864-71.

4 Geffroy N, Guedin A, Dacquet C, Lefebvre P. Cell cycle regulation of breast cancer cells through estrogen-induced activities of ERK and Akt protein kinases.
Mol Cell Endocrinol. 2005 Jun 15;237(1-2):11-23.

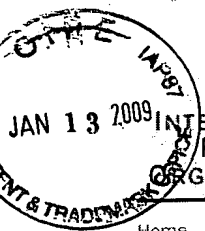
5 Caijo F, Mosset P, Gree R, Audinot-Bouchez V, Boutin J, Renard P, Caignard DH, Dacquet C. Synthesis of new carbo- and heterocyclic analogues of 8-HETE and evaluation of their activity towards the PPARs.
Bioorg Med Chem Lett. 2005 Oct 15;15(20):4421-6.

6 Bassène CE, Suzenet F, Hennuyer N, Staels B, Caignard DH, Dacquet C, Renard P, Guillaumet G.
Studies towards the conception of new selective PPARbeta/delta ligands.
Bioorg Med Chem Lett. 2006 Sep 1;16(17):4528-32.

7 E Blanc-Delmas, N Lebegue, V Wallez, V Leclerc, S Yous, P Carato, A Farce, C Bennejean, P Renard, D-H Caignard, V Audinot-Bouchez, P Chomarat, JA Boutin, N Hennuyer, K Louche, MC Camona, B Staels, L Pénicaud, L Casteilla, M Lonchamp, C Dacquet, P Chavatte, P Berthelot and D Lesieur
Novel 1,3-Dicarbonyl Compounds Having 2(3H)-Benzazolonic Heterocycles as PPAR α Agonists Bioorg Med Chem. 2006 Nov 15;14(22):7377-91.

8 Germain P, Staels B, Dacquet C, Speeding M, Laudet V.
Overview of nomenclature of nuclear receptors
Pharmacol. Rev. 2006 Dec, 58(4): 685-704. Review

9 Camona MC, Louche K, Lefebvre B, Pilon A, Hennuyer N, Audinot-Bouchez V, Fievet C, Torpier G, Formstecher P, Renard P, Lefebvre P, Dacquet C, Staels B, Casteilla L, Pénicaud L.
S 26948-1: a new specific peroxisome proliferator activated receptor gamma modulator with potent antidiabetes and antiatherogenic effects.
Diabetes. 2007 Nov; 56(11):2797-808.



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Search result: 1 of 1

(WO/2004/032967) ASSOCIATION BETWEEN A PPAR LIGAND AND AN ANTIOXIDANT AGENT AND USE THEREOF FOR TREATING OBESITY

Biblio. Data Description Claims National Phase Notices Documents

Latest bibliographic data on file with the International Bureau

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Chapter 2 Demand Filed: 23.04.2004

IPC: A61K 45/06 (2006.01)

Applicants: LES LABORATOIRES SERVIER [FR/FR]; 12, place de la Défense, F-92415 Courbevoie Cedex (FR) (All Except US).
CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE [FR/FR]; 3, rue Michel-Ange, F-75794 Paris Cedex 16 (FR) (All Except US).
CASTEILLA, Louis [FR/FR]; (FR) (US Only).
PENICAUD, Luc [FR/FR]; (FR) (US Only).
DACQUET, Catherine [FR/FR]; (FR) (US Only).
RENARD, Pierre [FR/FR]; (FR) (US Only).

Inventors: CASTEILLA, Louis; (FR).
PENICAUD, Luc; (FR).
DACQUET, Catherine; (FR).
RENARD, Pierre; (FR).

Agent: LABORATOIRES SERVIER; 12, place de la Défense, F-92415 Courbevoie Cedex (FR).

Priority Data: 02/12646 11.10.2002 FR

Title: (EN) ASSOCIATION BETWEEN A PPAR LIGAND AND AN ANTIOXIDANT AGENT AND USE THEREOF FOR TREATING OBESITY
(FR) ASSOCIATION ENTRE UN LIGAND DES PPAR ET UN AGENT ANTIOXYDANT ET UTILISATION DANS LE TRAITEMENT DE L'OBESITE

Abstract: (EN) The invention concerns an association containing one or more ligands of the peroxisome proliferator activated receptors and an antioxidant agent. The invention is applicable to medicines.

(FR) Association contenant un ou plusieurs ligands des récepteurs activés par les proliférateurs de peroxisomes et un agent antioxydant. Médicaments.

Designated States: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
African Regional Intellectual Property Org. (ARIPO) (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW)
Eurasian Patent Organization (EAPO) (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM)
European Patent Office (EPO) (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR)
African Intellectual Property Organization (OAPI) (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Publication Language: French (FR)

Filing Language: French (FR)

**(WO/2004/032967) ASSOCIATION BETWEEN A PPAR LIGAND AND AN
ANTIOXIDANT AGENT AND USE THEREOF FOR TREATING OBESITY**[Biblio. Data](#) [Description](#) [Claims](#) [National Phase](#) [Notices](#) [Documents](#)**Published International Application**

<u>Date</u>	<u>Title</u>		
06.05.2005	Correction of entry in Section I of the PCT Gazette (A1 18/2005)	view	download
22.04.2004	Initial Publication with ISR (A1 17/2004)	view	download

Related Documents on file at the International Bureau ([more information](#))

<u>Date</u>	<u>Title</u>		
30.05.2005	English Translation of International Preliminary Examination Report	view	download
11.04.2005	International Preliminary Examination Report	view	download
22.04.2004	FR 02/12646 11.10.2002 (Pr. Doc.)	view	download

INTERNATIONAL SEARCH REPORT

International Application No

PCT/FR 03/02986

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K45/06 A61K31/4439 A61K31/122 A61P3/04 A61P3/10

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, PAJ, WPI Data, BIOSIS, EMBASE, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 02/34259 A (FOURNIER LABORATORIES IRELAND) 2 May 2002 (2002-05-02) claims 1,3-5,8 page 6, line 29 - page 7, line 5 -----	1-3,5, 7-13
X	WO 97/28149 A (MERCK) 7 August 1997 (1997-08-07) claims 1,6,14 page 5, lines 33,34 page 10, lines 12-18 page 15, lines 16-33 -----	1-3,7-13
X	WO 02/064549 A (PFIZER PRODUCTS) 22 August 2002 (2002-08-22) claims 1,15 page 1, lines 3-7 page 13, line 18 - page 14, line 2 page 20, line 1 ----- -/-	1-3,7-25

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

A document defining the general state of the art which is not considered to be of particular relevance

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O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

G document member of the same patent family

Date of the actual completion of the international search

3 March 2004

Date of mailing of the international search report

10/03/2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Bocheïen, D

INTERNATIONAL SEARCH REPORT

Internat~~ional~~ Application No

PCT/FR 03/02986

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WO 02/060388 A (MERCK) 8 August 2002 (2002-08-08) claims 1,18 page 1, lines 6-10 page 24, line 22 - page 25, line 9 page 61, line 30 - page 62, line 14</p>	1-3,7-25
X	<p>WO 02/064094 A (MERCK) 22 August 2002 (2002-08-22) claims 1,33,34 page 1, lines 6-10 page 6, lines 16-29 page 33, lines 9-30</p>	1-3,7-25

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/TR 03/02986

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0234259	A	02-05-2002	AU 2176502 A	06-05-2002
			BR 0114701 A	18-11-2003
			CA 2426625 A1	02-05-2002
			CN 1471390 T	28-01-2004
			EE 200300165 A	16-06-2003
			WO 0234259 A1	02-05-2002
			EP 1328266 A1	23-07-2003
			NO 20031851 A	24-06-2003
			SK 5082003 A3	04-11-2003
			US 2004022778 A1	05-02-2004
WO 9728149	A	07-08-1997	AT 245622 T	15-08-2003
			AU 1856997 A	22-08-1997
			AU 721452 B2	06-07-2000
			AU 2115997 A	22-08-1997
			CA 2245529 A1	07-08-1997
			DE 69723680 D1	28-08-2003
			EP 0888278 A1	07-01-1999
			JP 2002503202 T	29-01-2002
			WO 9728115 A1	07-08-1997
			WO 9728149 A1	07-08-1997
			AU 712607 B2	11-11-1999
			AU 1858197 A	22-08-1997
			CA 2244831 A1	07-08-1997
			EP 1011651 A1	28-06-2000
			JP 2000504021 T	04-04-2000
			WO 9727847 A1	07-08-1997
			AU 719146 B2	04-05-2000
			AU 2250797 A	22-08-1997
			CA 2245524 A1	07-08-1997
			EP 0904079 A1	31-03-1999
			JP 2002515865 T	28-05-2002
			WO 9727857 A1	07-08-1997
			AT 236137 T	15-04-2003
			AU 708055 B2	29-07-1999
			AU 1856397 A	22-08-1997
			CA 2244836 A1	07-08-1997
			DE 69720429 D1	08-05-2003
			DE 69720429 T2	15-01-2004
			EP 0882029 A1	09-12-1998
			ES 2194179 T3	16-11-2003
			JP 2002503203 T	29-01-2002
			WO 9728137 A1	07-08-1997
			US 5859051 A	12-01-1999
			US 6090836 A	18-07-2000
			ZA 9700824 A	30-10-1998
			US 6020382 A	01-02-2000
			US 5847008 A	08-12-1998
			AU 719663 B2	11-05-2000
			AU 5615298 A	17-07-1998
			CA 2275394 A1	02-07-1998
			EP 0948327 A1	13-10-1999
			JP 2001511767 T	14-08-2001
			WO 9827974 A1	02-07-1998
			US 6160000 A	12-12-2000
			US 6515015 B1	04-02-2003
			US 6090839 A	18-07-2000

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/FR 03/02986

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0264549	A	22-08-2002	BR 0207285 A	10-02-2004
			CA 2438551 A1	22-08-2002
			EP 1360172 A1	12-11-2003
			WO 02064549 A1	22-08-2002
			US 2002165282 A1	07-11-2002
WO 0260388	A	08-08-2002	CA 2434491 A1	08-08-2002
			EP 1357908 A2	05-11-2003
			WO 02060388 A2	08-08-2002
			US 2002100854 A1	01-08-2002
WO 0264094	A	22-08-2002	CA 2437118 A1	22-08-2002
			EP 1366012 A2	03-12-2003
			WO 02064094 A2	22-08-2002

RAPPORT DE RECHERCHE INTERNATIONALE

Demande internationale No

PCT/FR 03/02986

A. CLASSEMENT DE L'OBJET DE LA DEMANDE

CIB 7 A61K45/06 A61K31/4439 A61K31/122 A61P3/04 A61P3/10

Selon la classification internationale des brevets (CIB) ou à la fois selon la classification nationale et la CIB

B. DOMAINES SUR LESQUELS LA RECHERCHE A PORTE

Documentation minimale consultée (système de classification suivi des symboles de classement)

CIB 7 A61K

Documentation consultée autre que la documentation minimale dans la mesure où ces documents relèvent des domaines sur lesquels a porté la recherche

Base de données électronique consultée au cours de la recherche internationale (nom de la base de données, et si réalisable, termes de recherche utilisés)

EPO-Internal, PAJ, WPI Data, BIOSIS, EMBASE, CHEM ABS Data

C. DOCUMENTS CONSIDERES COMME PERTINENTS

Catégorie *	Identification des documents cités, avec, le cas échéant, l'indication des passages pertinents	no. des revendications visées
X	WO 02/34259 A (FOURNIER LABORATORIES IRELAND) 2 mai 2002 (2002-05-02) revendications 1,3-5,8 page 6, ligne 29 - page 7, ligne 5	1-3,5, 7-13
X	WO 97/28149 A (MERCK) 7 août 1997 (1997-08-07) revendications 1,6,14 page 5, ligne 33,34 page 10, ligne 12-18 page 15, ligne 16-33	1-3,7-13
X	WO 02/064549 A (PFIZER PRODUCTS) 22 août 2002 (2002-08-22) revendications 1,15 page 1, ligne 3-7 page 13, ligne 18 - page 14, ligne 2 page 20, ligne 1	1-3,7-25
	-/-	

☒ Voir la suite du cadre C pour la fin de la liste des documents

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* Catégories spéciales de documents cités:

- *A* document définissant l'état général de la technique, non considéré comme particulièrement pertinent
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- *X* document particulièrement pertinent; l'invention revendiquée ne peut être considérée comme nouvelle ou comme impliquant une activité inventive par rapport au document considéré isolément
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- *Z* document qui fait partie de la même famille de brevets

Date à laquelle la recherche internationale a été effectivement achevée

3 mars 2004

Date d'expédition du présent rapport de recherche internationale

10/03/2004

Nom et adresse postale de l'administration chargée de la recherche internationale
Office Européen des Brevets, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Fonctionnaire autorisé

Bochelen, D

RAPPORT DE RECHERCHE INTERNATIONALE

Demande internationale No

PCT/FR 03/02986

C.(suite) DOCUMENTS CONSIDERES COMME PERTINENTS

Catégorie	Identification des documents cités, avec, le cas échéant, l'indication des passages pertinents	no. des revendications visées
X	<p>WO 02/060388 A (MERCK) 8 août 2002 (2002-08-08) revendications 1,18 page 1, ligne 6-10 page 24, ligne 22 - page 25, ligne 9 page 61, ligne 30 - page 62, ligne 14 -----</p>	1-3,7-25
X	<p>WO 02/064094 A (MERCK) 22 août 2002 (2002-08-22) revendications 1,33,34 page 1, ligne 6-10 page 6, ligne 16-29 page 33, ligne 9-30 -----</p>	1-3,7-25

RAPPORT DE RECHERCHE INTERNATIONALE

Renseignements relatifs aux numéros de familles de brevets

Demande internationale No

PCT/FR 03/02986

Document brevet cité au rapport de recherche		Date de publication	Membre(s) de la famille de brevet(s)	Date de publication
WO 0234259	A	02-05-2002	AU 2176502 A	06-05-2002
			BR 0114701 A	18-11-2003
			CA 2426625 A1	02-05-2002
			CN 1471390 T	28-01-2004
			EE 200300165 A	16-06-2003
			WO 0234259 A1	02-05-2002
			EP 1328266 A1	23-07-2003
			NO 20031851 A	24-06-2003
			SK 5082003 A3	04-11-2003
			US 2004022778 A1	05-02-2004
WO 9728149	A	07-08-1997	AT 245622 T	15-08-2003
			AU 1856997 A	22-08-1997
			AU 721452 B2	06-07-2000
			AU 2115997 A	22-08-1997
			CA 2245529 A1	07-08-1997
			DE 69723680 D1	28-08-2003
			EP 0888278 A1	07-01-1999
			JP 2002503202 T	29-01-2002
			WO 9728115 A1	07-08-1997
			WO 9728149 A1	07-08-1997
			AU 712607 B2	11-11-1999
			AU 1858197 A	22-08-1997
			CA 2244831 A1	07-08-1997
			EP 1011651 A1	28-06-2000
			JP 2000504021 T	04-04-2000
			WO 9727847 A1	07-08-1997
			AU 719146 B2	04-05-2000
			AU 2250797 A	22-08-1997
			CA 2245524 A1	07-08-1997
			EP 0904079 A1	31-03-1999
			JP 2002515865 T	28-05-2002
			WO 9727857 A1	07-08-1997
			AT 236137 T	15-04-2003
			AU 708055 B2	29-07-1999
			AU 1856397 A	22-08-1997
			CA 2244836 A1	07-08-1997
			DE 69720429 D1	08-05-2003
			DE 69720429 T2	15-01-2004
			EP 0882029 A1	09-12-1998
			ES 2194179 T3	16-11-2003
			JP 2002503203 T	29-01-2002
			WO 9728137 A1	07-08-1997
			US 5859051 A	12-01-1999
			US 6090836 A	18-07-2000
			ZA 9700824 A	30-10-1998
			US 6020382 A	01-02-2000
			US 5847008 A	08-12-1998
			AU 719663 B2	11-05-2000
			AU 5615298 A	17-07-1998
			CA 2275394 A1	02-07-1998
			EP 0948327 A1	13-10-1999
			JP 2001511767 T	14-08-2001
			WO 9827974 A1	02-07-1998
			US 6160000 A	12-12-2000
			US 6515015 B1	04-02-2003
			US 6090839 A	18-07-2000

RAPPORT DE RECHERCHE INTERNATIONALE

Renseignements relatifs aux familles de brevets

Demande internationale No

PCT/FR 03/02986

Document brevet cité au rapport de recherche		Date de publication	Membre(s) de la famille de brevet(s)		Date de publication
WO 0264549	A	22-08-2002	BR	0207285 A	10-02-2004
			CA	2438551 A1	22-08-2002
			EP	1360172 A1	12-11-2003
			WO	02064549 A1	22-08-2002
			US	2002165282 A1	07-11-2002
WO 0260388	A	08-08-2002	CA	2434491 A1	08-08-2002
			EP	1357908 A2	05-11-2003
			WO	02060388 A2	08-08-2002
			US	2002100854 A1	01-08-2002
WO 0264094	A	22-08-2002	CA	2437118 A1	22-08-2002
			EP	1366012 A2	03-12-2003
			WO	02064094 A2	22-08-2002

Translation

PATENT COOPERATION TREATY

PCT/FR2003/002986



PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PPAROX	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/FR2003/002986	International filing date (day/month/year) 10 octobre 2003 (10.10.2003)	Priority date (day/month/year) 11 octobre 2002 (11.10.2002)
International Patent Classification (IPC) or national classification and IPC A61K 45/06, 31/4439, 31/122, A61P 3/04, 3/10		
Applicant LES LABORATOIRES SERVIER		

<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>5</u> sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of _____ sheets.</p>	
<p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the report</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input type="checkbox"/> Certain observations on the international application</p>	

Date of submission of the demand 23 avril 2004 (23.04.2004)	Date of completion of this report 20 December 2004 (20.12.2004)
Name and mailing address of the IPEA/EP	Authorized officer
Facsimile No.	Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/FR2003/002986

I. Basis of the report

1. With regard to the elements of the international application:*

- ☒ the international application as originally filed
- ☒ the description:
pages _____ 1-9 _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____
- ☒ the claims:
pages _____ 1-25 _____, as originally filed
pages _____, as amended (together with any statement under Article 19
pages _____, filed with the demand
pages _____, filed with the letter of _____
- ☐ the drawings:
pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____
- ☐ the sequence listing part of the description:
pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language _____ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).

** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/FR 03/02986

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims		YES
	Claims	1-5, 7-15	NO
Inventive step (IS)	Claims		YES
	Claims	1-25	NO
Industrial applicability (IA)	Claims	1-25	YES
	Claims		NO

2. Citations and explanations

Reference is made to the following documents cited in the search report. The numbering given below will be used throughout the rest of the procedure:

D1: WO 02/34259 A (FOURNIER LABORATORIES IRELAND) 2 May 2002 (2002-05-02)

D2: WO 97/28149 A (MERCK) 7 August 1997 (1997-08-07)

D3: WO 02/064549 A (PFIZER PRODUCTS) 22 August 2002 (2002-08-22)

D4: WO 02/060388 A (MERCK) 8 August 2002 (2002-08-08)

D5: WO 02/064094 A (MERCK) 22 August 2002 (2002-08-22)

The relevant passages are those cited in the search report.

1. Prior art:

Document D1 describes compositions comprising an agonist of PPAR alpha or gamma such as a thiazolidinedione in combination with a benzoquinone (coenzyme Q10).

Document D2 describes compositions comprising an agonist of PPAR delta having an affinity for the alpha and gamma sub-types, in combination with vitamin C or E.

Document D3 describes compositions comprising an agonist of PPAR alpha, optionally in combination with an antioxidant agent for treating obesity and diabetes.

Document D4 describes compositions comprising ligands for PPAR gamma and alpha, optionally in combination with rosiglitazone and an antioxidizing agent for treating obesity and diabetes.

Document D5 describes compositions comprising ligands for PPAR gamma and alpha, optionally in combination with an antioxidant agent for treating obesity and diabetes.

2. Novelty:

Claims 1-5 and 7-15 are not novel over documents D1 to D5.

3. Inventive step:

The use of ligands for PPAR in association with an antioxidant agent for treating obesity is known (see D1 to D5). The selection of a group of patients having a predetermined body weight index, or patients whose obesity is due to a treatment such as for diabetes, is not considered inventive. Therefore, the subject matter of claims 16-25 is not inventive.